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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

HINES, JANA A

ART UNIT

PAPER NUMBER

1645

DATE MAILED: 08/23/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/426,776

Applicant(s)

DING ET AL.

Examiner

Ja-Na A Hines

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 May 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9, 11-13, 15-17 and 26-29 is/are pending in the application.
- 4a) Of the above claim(s) 7-9, 11-13 and 26-29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 15-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in Paper No. 8 is acknowledged. Claims 7-9, 11-13 and 26-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected groups, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8. The traversal is on the ground(s) that the particular secretory sequence enables the secretion of different proteins in an arrays of hosts, thus the other groups can be practiced in conjunction with Group I. This is not found persuasive because the products are distinct as claimed because they have different structures. Group I is drawn to an isolated nucleic acid encoding a secretory sequence; however the other claims are drawn to different nucleic acids encoding different products such as fusion proteins and other desired proteins. Each group has a different function, effect and is capable of use without the other. For instance, the isolated nucleic acid product of claims 7-9 can encode a fusion protein, while group I cannot. The elected group cannot express fusion protein. Each group has a different structure, produces different effects and has a different function from the other group. Therefore, the products of the inventions are distinct as claimed. The requirement is still deemed proper and is therefore made FINAL.

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Amendment Entry

2. Applicants amendments filed June 4, 2002 has been entered. Examiner acknowledges amendments to the specification. Claims 2, 8 and 13 have been amended. Claims 1-9, 11-13, 15-17 and 26-29 are under consideration in this office action, however claims 7-9, 11-13 and 26-29 have been withdrawn from consideration in view of the restriction requirement.

Priority

3. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

Specification

4. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

5. The attempt to incorporate subject matter into this application by reference to 08/596,405 and 09/081,767 at page 27 line 4 and the like as recited within the instant specification are improper because a mere reference to another application, is not an incorporation since the documents do not appear to be published. However, if the

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applications have been published, the patent number needs to be entered in place of the serial number.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 1-6 and 15-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to variants of said amino acid sequence that comprises conservative replacements thereof. The written description in this case only sets forth the specific amino acid sequence of SEQ ID NO:10, therefore the written description is not commensurate in scope with the claims drawn to variants thereof. There is no guidance as to what variants can or cannot be used that satisfy the claims. The specification does not include structural examples of variants thereof. There are no representative examples of variants thereof. Thus, the resulting variant could result in complexes not taught and enabled by the specification.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the

'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

With the exception of specifically named SEQ ID NO:10, the skilled artisan cannot envision the detailed structure of the variants thereof, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. Furthermore, *In The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of by only their functional activity does not provide an adequate description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules falling within the scope of the claimed genus.

Therefore only the recited sequence, SEQ ID NO:10 and not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

7. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Acronyms like COS, CHO, and EPC must be spelled out when used for the first time in a chain of claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by LaFleur et al. LaFleur et al., teach the derivation of oocyte and egg proteins from parenteral vitellogenins in *Fundulus heteroclitus* and vitelline envelope protein precursors and in particular the vitellogenin II precursor mRNA. See EMBL: U70826 submitted the 15 September 1996. It should be noted that since the claim recites comprising which is open language, the instant art applies since the claimed sequence is comprised within the isolated nucleic acid sequence.

Thus, LaFleur et al., teach a nucleic acid comprising a nucleotide sequence encoding a secretory signal comprising the amino acid sequence SEQ ID NO:10 or variants of said amino acid sequence that comprise conservative replacements thereof that retain the biological activity of directing secretion and cleavage of the secretory signal.

9. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Lim et al. Lim et al., teach cloning of full length *Oreochromis aureus* vitellogenin cDNA and its deduced primary structure. See Accession numbers: AF017250 and AAD01615 which were both submitted 5 August 1997. It should be noted that since the claim recites

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comprising which is open language, the instant art applies since the claimed sequence is comprised within the isolated nucleic acid sequence.

Thus, Lim et al., teach a nucleic acid comprising a nucleotide sequence encoding a secretory signal comprising the amino acid sequence SEQ ID NO:10 or variants of said amino acid sequence that comprise conservative replacements thereof that retain the biological activity of directing secretion and cleavage of the secretory signal.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 3-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lim et al., as applied to claim 1 above, and further in view of Lee et al. Lim et al., has been discussed above, however, Lim et al, does not teach expression in eukaryotic or prokaryotic cells. Lee et al., teach the vitellogenin gene expression in eukaryotic *Oreochromis aureus* has already been documented (page 75). The authors teach using vitellogenin cDNA and cloning it into vectors and transducing such into prokaryotic *E.coli* cell lines (page 76).

Therefore it would have been prima facie obvious at the time of applicants invention to use a nucleotide sequence comprising the secretion signal sequence as taught by Lim et al., and expressing it in either a eukaryotic or prokaryotic cell as taught

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by Lee et al., when Lee et al., teach expression in both eukaryotic and prokaryotic cells. One of skill in the art would have a reasonable expectation of success when vitellogenin expression in eukaryotic cells have already been previously performed by those of skill in the art. Moreover, no more than routine skill would have been required to use the secretion signal sequence which is known in the art to direct secretion and capable of having said expression induced by hormones when the art already teaches it expression and inducement in recombinant eukaryotic cells.

11. Claims 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lim et al., as applied to claim 1 above, and further in view of Yarranton. Lim et al., has been discussed above, however Lim et al., does not teach using the sequence secretion signal peptide within the expression systems. Yarranton teach mammalian recombinant proteins: vectors and expression systems. Yarranton teach that *E.coli* expression systems have been widely employed for use with heterologous proteins wherein the highly efficient system produces recombinant proteins (page 133). Advances in the production of soluble active proteins have been achieved by fusing N-terminal signal sequence to the protein. Signal sequences processing is accurate and efficient and has high yield (page 134). It is encouraged that the signal sequence is removed thereby allowing the protein to fold correctly (page 134). Thus, particular charged residues within the N-terminus of the mature protein close to the signal peptide may prevent translocation, thus the authors discuss removal of those charged residues (page 134). A variety of mammalian cell expression systems are available for the

transient expression of recombinant genes or long-term production cell lines (page 134).

Table 3 shows mammalian cell expression systems including Chinese Hamster Ovary (CHO) cells. The authors also teach yeast expression systems and viral vectors.

Therefore it would have been prima facie obvious at the time of applicants invention to use a nucleotide sequence comprising the secretion signal sequence as taught by Lim et al., to aid in directing secretion of the protein by a recombinant vector and host cell as taught by Yarranton. One of skill in the art would have a reasonable expectation of success in employing the signal sequence of Lim et al., since Yarranton teaches signal sequences aid in the secretion of heterologous proteins. Moreover, no more than routine skill would have been required to use the signal sequence of Lim et al., which is known in the art to direct secretion as part of a heterologous protein, when the art teaches incorporating nucleic acid into recombinant vectors and host cells to produce such proteins.

Prior Art

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Ding et al., (1994) teach the enhancing effect of cortisol on estradiol-induced Vg Gene transcription. Lim et al., (1991) teach hormone induced gene expression of vitellogenin gene expression.

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13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines *Av*

August 14, 2002

Nita Minnifield
NITA MINNIFIELD
PRIMARY EXAMINER
8/22/02